

PRP: Assessing Its Safety and Efficacy

As use of platelet-rich plasma grows in popularity, a dermatologist undertakes a review of the current evidence.

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What is the safety and efficacy of platelet-rich plasma (PRP) in adults pertaining to wound healing and aesthetic rejuvenation? As use of PRP expands, a growing number of physicians and patients seek to answer this question. Barring large-scale clinical trials, a systematic literature review offers the best chance of answering this question. Per the Cochrane collaboration, a systematic review evaluates and compiles the findings of multiple clinical trials and provides best evidence to address the chosen research question. Conclusions can then be made and future recommendations suggested.

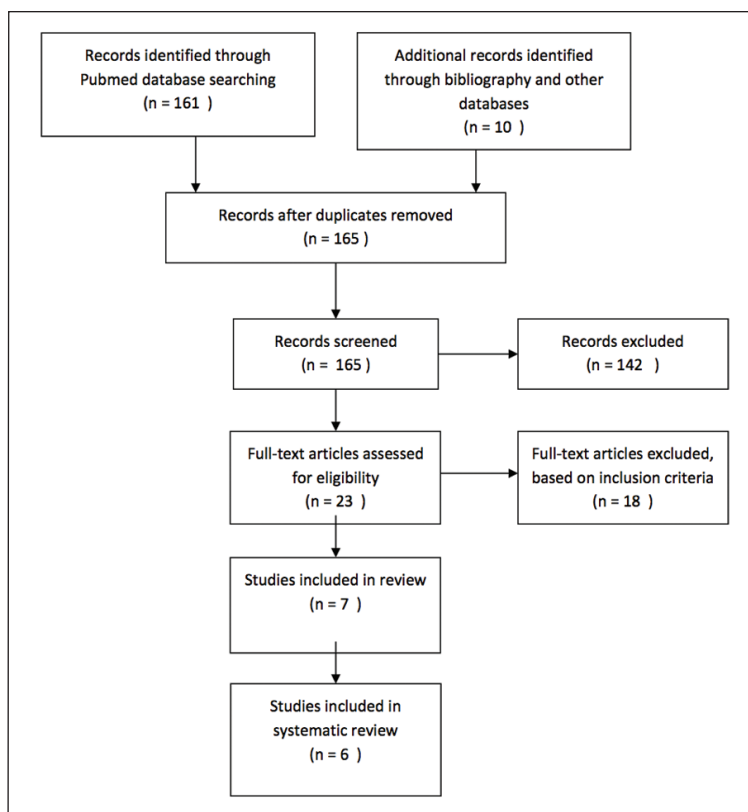
SEARCH STRATEGY

A comprehensive search of the current literature was undertaken using three databases—Cochrane Library, Medline via the Pubmed interface, and Google scholar—for an extensive review. The search parameters were limited to all English Language articles from 2006 to 2016, excluding animal studies, in vitro studies, and articles with no measureable endpoint.

The search strategy was designed to select all relevant articles via Mesh terms combined with key text terms to address our research question. Different constructs of search terms were formed by the implementation of truncation of the following terms: PRP wound healing, PRP facial rejuvenation, PRP, platelet-rich plasma, platelet preparations, PRFM platelet-rich fibrin matrix, growth factors, platelet therapy, platelet facial platelet wound healing, platelet plastic surgery AND facial rejuvenation or aesthetic rejuvenation or wound healing

SEARCH OUTCOME

Initial search yielded 552 publications from Pubmed, nine



from Cochrane Library, and 1,470 from Google Scholar. The search term was refined further to identify relevant articles, adhering to the steps of Prisma 2009. A review of the title and abstract of these papers was undertaken to determine their relevance to our research question, and this then yielded 23 potentially relevant papers. Scanning the references of these papers yielded further studies. Next, an in-depth analysis of these papers was carried out to ascertain the level of evidence, quality, and whether they met all of our inclusion and exclusion criteria. Six systematic reviews and one critical review were eventually extracted.

TABLE 1. DATA ANALYSIS

Author and date	Intervention	Sample size	Outcome Measure	Evidence level	Study reference	Weakness
Martinez et al 2009	Tissue regeneration	20 RCTs	Oral and maxillofacial surgery, skin ulcers and surgical wounds. Bone biopsy Gingival index Complete epithelialization, TGF-beta Edema and ecchymosis via photography	1	1	20 quality RCTs found, based on Jadad scale which is out-dated. Publication bias as no attempt to look at unpublished data. Results not reproducible. Methodological limitations due to heterogeneity and lack of description. Allocation concealment is questionable in the studies. Little data on safety. Small study size with large confidence intervals.
Villela et al 2010	Diabetic Ulcer	18 studies	Number of healed ulcers	1	2	Research question was too broad. Eligibility criteria was not defined. Heterogeneity and methodological flaws, example volume of blood used varied from 20 to 240ml. Poor reporting on the review process. Lack of data on the included studies, example intervention, control and treatment regimen.
Carter et al 2011	Wound healing in 3 main types of wounds, acute primary closure, acute secondary closure and chronic wounds.	24 papers (21 clinical studies and 3 systematic reviews)	PRP can positively impact wound healing, pain, and infection in both acute and chronic cutaneous cases. Complete wound healing, superficial infection and pain reduction. Wound area reduction, Wound depth, healing rate, time to heal, complications, Quality of life.	1	3	Wide variation in quality of studies and a risk of publication bias. Outcome measures for wound healing was too diverse.

TABLE 1. DATA ANALYSIS (CONTINUED)

Author and date	Intervention	Sample size	Outcome Measure	Evidence level	Study reference	Weakness
Taylor et al 2011	Tendon and ligament injuries	13	Constant score, MRI, serum cytokine concentration via Elisa assay,	1	4	From the studies, only 3 were RCTs. Wide variation in the method of collection, preparation, administration amongst the studies. Sample size was small in majority, with limited data and short term followup.
Wang et al 2014	PRP for treatment of acute wounds (meta-analysis)	13 articles involving 982 patients	Wound healing time, length of hospital stay, incidence of disturbed wound healing, post traumatic pain, wound infections. Findings: Use of PRP can shorten acute wound healing time and length of hospital stay, reduce the incidence of disturbed wound healing and blood products transfusion and alleviate post-traumatic pain, and wound infections.	1	7	Good statistical analysis with use of wide range of RCTs in the study. Role of publication bias. Wide variation in the method of collection, preparation, administration amongst the studies.
Leo et al 2015	Aesthetic Dermatology	22 manuscripts	Outcome measure not detailed. Benefit in scar revision, androgenic alopecia, post laser recovery and rejuvenation.	1	5	Bias Results not reproducible. Several studies lack controls, split-face comparisons, To better evaluate PRP efficacy and reduce inter-subject variability. Studies were often small scale, with few subjects. Lack of studies evaluating different forms of PRP and variation in the PRP collection process, which leads to difficulty in comparing studies.
Sclafani et al 2015	Facial rejuvenation and wound healing	61 reports, divided into in vitro, animal studies and clinical studies.	Varied outcome measures, positive effect on cellular changes, wound healing and facial rejuvenation.	5	6	Limitation: Reports varied widely in measurable endpoints.

Steps in a systematic review, as per Cochrane:

1. Identify your research question.
2. Search for studies.
3. Define inclusion and exclusion criteria.
4. Extract studies that fulfill the above criteria.
5. Perform data analysis of selected studies.
6. Evaluate the degree of bias of the above.
7. Present findings and assess quality and level of evidence.

Research question:

What is the safety and efficacy of platelet-rich plasma in adults pertaining to wound healing and aesthetic rejuvenation?

Target population – Adults

Intervention - Aesthetic Rejuvenation and Wound Healing with platelet-rich-plasma

Outcome(s) – Safety, Efficacy

CONCLUSION

Efficacy. Of the six systematic reviews and one critical review, five evaluated various types of wound healing from post-surgical ulcers, sports related, and two evaluated aesthetic rejuvenation. Studies varied in design, size, and power, hence this lack of uniformity results in complexity in comparison, and poor validity and reproducibility of findings. Reports varied in outcome measures.

In wound healing, common parameters used were complete wound healing, wound area reduction, wound depth, healing rate, time to heal, complications, example wound infection, quality of life, and pain reduction. As wounds cover a wide spectrum, from medical to post surgical, and consist of a wide degree of variation, the studies unfortunately did not indicate a detailed description of the type of wounds investigated to correct for inter wound variability.

In aesthetic rejuvenation, common parameters used were subjective doctor and patient evaluation, photo reviews, and objective skin biopsy, trichoscan hair measurements, etc. Noting the above variation in outcome measures, findings tend to lack statistical power. Several studies lacked controls and split-face comparisons. Studies were often small scale, with few subjects.

There is a high likelihood of publication bias favoring positive results with the use of PRP in both cases, which demonstrated positive effects on cellular changes, wound healing and aesthetic rejuvenation. Many of the studies demonstrated results that were difficult to quantify objectively. PRP treatment protocol lacked standardization for extraction, injection, dosing, and volume. Lack of studies evaluating different forms of PRP and variation in the PRP collection process, which leads to difficulty in comparing studies.

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SEARCH PARAMETER

1. Search (("Platelet-Rich Plasma"[Mesh] AND "last 10 years"[PDat] AND Humans[Mesh])) AND (facial rejuvenation or wound healing) – 552 results on Pubmed
2. Search (safety or efficacy) AND "Platelet-Rich Plasma"[Mesh] Sort by: Relevance Filters: published in the last 10 years; Humans – 325 results on Pubmed
3. "Platelet-Rich Plasma"[Mesh] AND "last 10 years"[PDat] AND Humans[Mesh])) AND (facial rejuvenation or wound healing)) AND "last 10 years"[PDat] AND Humans[Mesh])) AND (systematic review or critical review) – 161 results on Pubmed
4. Search (((safety or efficacy) AND "Platelet-Rich Plasma"[Mesh]) AND "last 10 years"[PDat] AND Humans[Mesh])) AND systematic review Sort by: Relevance Filters: published in the last 10 years; Humans – 102 results on Pubmed
5. Search ((((((safety or efficacy) AND "Platelet-Rich Plasma"[Mesh]) AND "last 10 years"[PDat] AND Humans[Mesh])) AND systematic review) AND "last 10 years"[PDat] AND Humans[Mesh])) AND WOUND HEALING Sort by: Relevance Filters: published in the last 10 years; Humans – 39 results on Pubmed
6. Search (((((((safety or efficacy) AND "Platelet-Rich Plasma"[Mesh]) AND "last 10 years"[PDat] AND Humans[Mesh])) AND systematic review) AND "last 10 years"[PDat] AND Humans[Mesh])) AND AESTHETIC REJUVENATION Sort by: Relevance Filters: published in the last 10 years; Humans – 0 results on Pubmed
7. 'Platelet rich plasma' – 9 results on Cochrane
8. 'platelet rich plasma and wound healing and facial rejuvenation' – 1470 results on google scholar
9. 'platelet rich plasma and (wound healing or aesthetic rejuvenation)' – 612 results on google scholar
10. 'platelet rich plasma and wound healing and aesthetic rejuvenation' – 589 results on google scholar

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INCLUSION CRITERIA

Adults > 19 years old
 Skin rejuvenation or Wound healing
 Timeframe for 2006 to 2016
 English language publications
 Highest quality papers with level 1 evidence

EXCLUSION CRITERIA

Animal studies
 In vitro studies
 Articles with no measurable endpoint

ABBREVIATIONS:

RCT: randomized controlled trials
 PRP: Platelet rich plasma

Safety. On the aspect of safety, PRP is superior to filler agents, with self-limiting minor side effects of swelling, erythema and bruising as per QMUL module 8 coursework. The above studies have not reported any long-term or permanent side effects.

Clinical application. With reference to the research question, our findings show that although results are encouraging, high level evidence and high quality RCTs are still lacking. That said, the evidence for wound healing appears to be more substantial than for aesthetic rejuvenation as seen by the quality, design, and number of RCTs.

There is still a wide variation in the types and uses of platelet preparation, with no universal standard. Combination of PRP with other modalities is a big scope for future evaluation, specifically the choice, dosing, sequencing, interval, and frequency.

Large robust RCTs are needed, however a suitable split-face intervention as a control to PRP has yet to be established. Another challenge would be the fact that pharmaceutical companies would hesitate to fund a trial with no intellectual property rights. ■

Dr. Daniel Chang specializes in Aesthetic and Regenerative Medicine and is a Key Opinion Leader and Regional Trainer. Dr. Chang founded Asia Aesthetic Academy in 2015 and has developed a number of signature treatments, including the DC 3D-Dreamlift and the DC 3D-Noselift. He maintains a Korean Aesthetics site and can be reached at drdanielchang.com



Martinez-Zapata MJ, Marti-Cavajal A, Sola I, et al. Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review. *Transfusion*. 2009;49(1):44-56.

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Carter, Marissa J, Carelyn P. Fylling, and Laura KS Parnell. "Use of platelet rich plasma gel on wound healing: a systematic review and meta-analysis." ePlasty. Open Access. *Journal of Plastic Surgery* 11 (2011).

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Leo, Michael S., et al. "Systematic review of the use of platelet rich plasma in aesthetic dermatology." *Journal of cosmetic dermatology* 14.4 (2015): 315-323.

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